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CLAIMS



- A process for the preparation of small particles through precipitation, which process
 employs a fluid solution comprising a solvent and solute to be precipitated and a nongaseous antisolvent, said solvent being soluble in or miscible with the antisolvent and said
 solute being substantially insoluble in the antisolvent, wherein the process comprises the
 successive steps of:
 - feeding a stream of the fluid solution and a stream of the antisolvent into a mixing zone where both streams are thoroughly mixed to achieve a condition of super saturation whilst ensuring that hardly any nucleation occurs during the mixing;
 - b. feeding the resulting mixture of the fluid solution and the antisolvent into a nucleation zone allowing nucleation to commence;
 - c. allowing the nuclei formed in the nucleation zone to grow to particles with a volume weighted average diameter of no more than 50 μ m, preferably of no more than 7 μ m;
 - d. collecting the particles and separating them from the antisolvent; and wherein during or following step b., and prior to step d. additional antisolvent is admixed to the mixture of the fluid solution and the antisolvent.
- 2. The process according to claim 1, wherein during or following step b., and prior to step d. additional antisolvent is admixed to the mixture of the fluid solution and the antisolvent.
 - 3.2. The process according to claim 12, wherein the additional antisolvent is admixed after the precipitated particles have grown to a volume weighted average diameter of at least 0.1 μ m, preferably of at least of at least 0.4 μ m
 - 4.3. The process according to claim 12 or 23, wherein the antisolvent is admixed at least 1 second after completion of step a., preferably at least 3 seconds after completion of step a.
- <u>5.4.</u>The process according to any one of claims 1-<u>3</u>4, wherein the ratio of the solution flow rate to antisolvent flow rate in step a. is between 5:1 and 1:10.
 - 6.5. The process according to any one of claims 1-45, wherein the collected particles, when reaching the end of the nucleation zone or immediately prior to the admixture of additional antisolvent, contain at least 1 wt.% solvent, preferably at least 10 wt.% solvent.

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- 7.6. The process according to any one of claim 1-52-6, wherein the additional antisolvent is admixed in an amount effective to reduce the solvent content of the collected particles to less than 1 wt.%, preferably to less than 0.01 wt.%.
- <u>8.7.</u>The process according to any one of claims 1-67, wherein less than 25%, preferably less than 10% of the nuclei formed in the process are formed in the mixing zone.
- 9.8. The process according to any one of claims 1-78, wherein the residence time within the mixing zone is less than 15 seconds, preferably less than 1 second.
 - 10.9. The process according to any one of claims 1-89, wherein the mixing energy applied in the mixing zone exceeds 1 J/kg and preferable more than 10J/kg.
- 15 <u>41.10.</u> The process according to any one of claims 1-<u>912</u>, wherein the residence time within the nucleation and growth zone is at least 3 seconds, preferably at least 60 seconds.
 - <u>12.11.</u> The process according to any one of claims 1-<u>1011</u>, wherein the solution comprises between 0.0001 and 30 wt.%, preferably between 0.1 and 5 wt.% of the solute.
 - 13.12. The process according to any one of claims 1-112, wherein the antisolvent is a supercritical or nearcritical fluid.
 - 14.13. The process according to any one of claims 1-123, wherein the particles obtained from step c. have a particle size distribution with a standard deviation of less than 50% of the volume weighted average particle size, preferably of less than 20% of the volume weighted average particle size.
- 15.14. The process according to any one of claims 1-134, wherein at least 10 wt.%,
 preferably at least 50 wt.% of the solute present in the stream of the fluid solution of step
 a. is recovered in the particles obtained in step d.

